REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on 9/22/06, and the references cited therewith. Applicants gratefully acknowledge that the new oath has been accepted and made of record and that the objection to claim 15 has been withdrawn pursuant to Applicants' amendment. Applicants further acknowledge that the earlier 102(a) rejection has been withdrawn because the declaration filed on June 28, 2006, was sufficient to overcome the reference.

Currently claims 1, 2, 7, 10, 12-17 and 19 are amended, claims 3, 5, 8, 9, 11, and 18 are canceled; as a result, claims 1, 2, 4, 7, 10, 12-17, and 19 are now pending in this application.

§ *102 Rejection of the Claims*

Claims 17 and 18 were rejected under 35 USC § 102(b) as being anticipated by CA 2213780 (the '780 publication). Claim 18 has been canceled, and claim 17 has been amended to clarify the differences between the claimed invention and the prior art. The Office Action noted that Applicants asserted that the '780 application contained no recitation use of human cells; in fact, the '780 inventor stated that human cells would need to be tested to see if they would work. Therefore, Applicants' addition of the term "human" and "hNT cells" to the claim overcomes that rejection.

In addition, the '780 inventor only disclosed dopaminergic cells used in a rodent Parkinson's Disease model, not any other neurodegeneration model, and specifically not a stroke model. Therefore, this aspect of the reference cannot be used to reject claim 17 which now recites hNT neuronal cells (not generally considered dopaminergic cells) and treatment of stroke (a different affliction in a different part of the brain). The other possible uses in the '780 publication were merely hypothetical.

The Office Action quoted the part of MPEP (§ 2121.01), for the proposition that a reference is enabling is the public was in possession of the claimed invention before the date of the invention and that such possession is effected *if one of ordinary skill in the art* could have

combined the publication's description of the invention with his/her own knowledge to make the claimed invention. In response, the Applicants note that ordinary-art skilled scientists in this area are quite skeptical of any report, and certainly of any report of one specialized test purporting to prove the utility of other tests. Because of this known skepticism, the '780 inventor placed the caveat that "*it is necessary to show that they* [the human neural cells] *can be generated from human nasal epithelium* (emphasis added). Furthermore, the '780 publication only discloses treatment of the rodent Parkinson's Disease model, not stroke nor treatment in humans nor treatment with a human-derived neuronal cell. When the Applicants argue that the differing cell types and non-human animals do not provide enablement, Applicants are not "suggesting the non-enablement of their own method claim." That is because actual human data is given herein for the first time. Earlier rodent experiments while successful in animals, have a low probability of success in the human.

In order to anticipate claim 17, the '780 reference is required to disclose each and every limitation in the exact same way as recited in the claim. The '780 reference does not teach any of the following: 1) a method of replacing a human's nervous system nerves lost to stroke, 2) the administration of hNT neuronal cells, 3) use of at least 2 million hNT cells, and 4) administration into a plurality of brain sites. Therefore, this rejection should be withdrawn.

§ 103 Rejection of the Claims

Claims 1-4 were rejected under 35 USC § 103(a) as being unpatentable over the Weiss patent (U.S. 5,851,832 - the '832 patent) in view of Sanberg et al. (1997) and further in view of Grabowski et al. (1994) as set forth at pages 6-9 of the prior office action. Claim 1 has been amended and claim 3 has been canceled.

First, to establish a *prima facie* case of obviousness under 35 U.S.C. §103, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Third, the cited prior art references must teach or suggest all of the claim limitations. Furthermore, the suggestion to make the claimed combination and the reasonable expectation of

success must both be found in the prior art, not based upon the Applicants' disclosure. A failure to meet any one of these criteria is a failure to establish a *prima facie* case of obviousness. MPEP §2143.

The Office Action reiterates that the '832 patent discloses treatment of neurodegenerative disease (specifically Parkinson's Disease) and brain injuries and further disclosed in the Background. The Office Action also reiterates that Sanberg et al reference suggest that a greater overall number of transplanted cells is desirable in rodents and will produce a better outcome. Moreover, the Office Action states that Grabowski suggests that a longer delay following ischemic injury prior to the transplantation surgery is desirable. The Office Action concludes that all three references used widely-accepted rodent models for stroke, so the skilled artisan would have a reasonable expectation of success for treating stroke in humans.

As shown above, Applicants have modified the claims to recite the treatment of humans using hNT cells at multiple brain sites. The claims still recite the treatment of stroke and the use of at least 2,000,000 cells. The following discusses the references in the light of the current claims.

Viewing the '832 reference as a whole, one can see that both rodent (Examples 1-8) and primate cells were processed to produce neurospheres and their progenies, including nerve cells and other nervous tissue cells, not hNT neuronal cells. In addition, some rodent models were implanted with either embryonic or adult-derived nervous tissue. Moreover, there is a hypothetical example of a "patient" with non-specified "neurodegenerative disease" receiving fetal cells (Example 14). Examples 16, 17 and 18 are all hypothetical examples.

As with the '780 publication, there is no example of successful transplantation into humans, just rodent models which do not have a reasonable expectation of success in providing therapeutic benefit in humans. Thus, although the '832 patent alleges human treatment of neurodegenerative disorders, it provides no details such as are claimed by Applicants. There is no teaching or suggestion of hNT neuronal cells, let alone the amount of at least 2 million cells or administration into a plurality of brain sites.

The Sanberg et al teachings are based on the implantation of hNT cells in an animal model, and do not provide a reasonable expectation of success in humans. The Office Action (page 8) states that Sanberg et al "clearly suggests that a greater overall number of transplanted

cells is desirable and will produce a better outcome." In response, Applicants aver that Sanberg et al does not disclose "at least 2 million hNT neuronal cells," but at best the phrase "at least." Moreover, Sanberg et al do not disclose other important limitations in the claims, including the delivery into a plurality of brain sites.

The third reference is Grabowski et al disclosing a rodent model and a source of cells that is no longer claimed. Furthermore, while Grabowski alleges that longer delay in administering the cells (as long as 3 months), that limitation only appears in claim 4, not independent claim 1. The Office Action also suggests that the arguments of nonenablement of this and other references suggest "nonenablement of their own method claim." In response, Applicants note that they are the first to demonstrate successful use in humans in their specification, thus enabling the instant claims. Grabowski also does not disclose or suggest hNT neuronal cells, at least 2 million cells, or administration into a plurality of brain sites.

Because the combination of references fails to teach every limitation of the current claims 1-3, this ground for rejection appears to be moot and may be withdrawn.

Second § 103 Rejection of the Claims

Claims 7-19 were rejected under Section 103 over Sanberg and Borlongan (1996), in view of the '832 patent and further in view of Uchida (1995).

The Office Action states that Sanberg and Borlongan reported cognitive function in rats transplanted with hNT cells or striatal cells, similar to what was observed when fetal striatal cells were used in treating neurodegenerative diseases such as Huntington's. The Applicants believe that these proofs only apply to rodent models for stroke and Huntington's using hNT cells or striatal cells. There is no recitation or suggestion of the claimed amounts or administration to multiple brain sites in humans.

The Office Action next notes that Uchida et al is cited to prove that transplanted cells have the capacity to migrate to distant sites. The Office Action goes on to state that migrating cells in the prior art would render obvious claim 15, wherein it is recited that the cells are implanted "into a location from which the neuronal cells migrate to the damaged area." Importantly the Uchida reference also states that "[i]t cannot be ruled out that the 'distant' cells

were *deposited at their sites during implantation* (emphasis added)." Therefore, the teachings of Uchida are inconsistent and cannot be used to support the use of Uchida for the proposition that any transplanted cells can migrate to distant sites. Picking one of the Uchida statements over the other may even be the improper use of hindsight. Furthermore, Uchida fails to disclose or suggest at least 2 million cells or hNT neuronal cells that also are recited in currently amended claim 15.

Taking all the references together, none teach the use of hNT cells to treat stroke in humans, nor do they teach or suggest the proper dosage or implantation into a plurality of brain sites. Therefore, the combination of references fails to disclose all the elements of the instant claims. Thus, this rejection has been rendered moot and can be withdrawn.

35 USC § 112, First Paragraph

The Office Action found no support for the newly amended phrase "hemorrhagic or thrombotic" stroke. This rejection is rendered moot by Applicants' deleting the phrase from the claims. Therefore, Applicants respectfully request that this ground for rejection be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (480-344-7745) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 50-3956.

Respectfully submitted,

By their Representatives,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is transmitted by facsimile to the United States Patent office to the number 571-273-8300 on this 22 day of January, 2007.

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